

Burst Spinal Cord Stimulation in a Rat Model of Chronic Neuropathic pain

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In summary, the results presented in this academic thesis show that a more complex relationship defines the interplay between parameters of Burst SCS, the charge delivered to the spinal cord, and its analgesic efficacy. Burst SCS exhibits a delayed anti-nociceptive effect after onset of stimulation, and a delayed washout of analgesia after stimulation is turned off, as compared with Tonic SCS. We also found, in a well-established chronic neuropathic animal model, that the analgesic effect of both Burst SCS and Tonic SCS is mediated via spinal GABAergic mechanisms. In a behavioral experiment, we were able to demonstrate that Burst-SCS specifically affects, much more than Tonic-SCS, the processing of cognitive-motivational aspects of pain. Lastly, we demonstrated with functional Magnetic Resonance Imaging that both Tonic SCS and Burst SCS increase BOLD-signals in brain regions associated with cognitive-emotional aspects of pain. Yet, Burst SCS induces a more profound effect in these brain areas. Mechanism based insights and experimental studies as described in this thesis can lead to further optimization of the Burst-paradigm and eventually lead to better treatment of neuropathic pain in patients (CRPS/FBSS).

De resultaten van deze academische thesis laten zien dat er een complexe relatie bestaat tussen het analgetische effect en de parameters van burst ruggenmergstimulatie. Preklinische gedragstesten hebben uitgewezen dat er bij burst ruggenmergstimulatie, vergeleken met tonische ruggenmergstimulatie, een vertraagde wash-in van het analgetische effect optreedt. Daarnaast hebben wij, in een gerenomeerd diermodel voor chronisch neuropatische pijn, aangetoond dat Gamma-aminoboterzuur (GABA)-erge mechanismen ten grondslag liggen aan het analgetische effect van zowel burst ruggenmergstimulatie als tonische ruggenmergstimulatie. Aan de hand van een innovatieve nieuwe gedragstest in combinatie met functioneel Magnetic Resonance Imaging (MRI) onderzoek hebben wij aangetoond dat zowel burst ruggenmergstimulatie als tonische ruggenmergstimulatie verhoogde hersenactiviteit teweegbrengen in breinregionen betrokken bij het verwerken van cognitief-emotionele aspecten van pijn. Echter, voor burst ruggenmergstimulatie was de desbetreffende activiteit intenser en meer wijdverspreid. Samengevat, burst ruggenmergstimulatie heeft overeenkomsten alswel verschillen met tonische ruggenmergstimulatie. Het is belangrijk dat de verschillen in de toekomst verder onderzocht worden om op deze manier de analgetische effectiviteit van burst ruggenmergstimulatie optimaal te kunnen benutten.